The opinion in support of the decision being entered today was <u>not</u> written for publication and is <u>not</u> binding precedent of the Board.

Paper No. 20

#### UNITED STATES PATENT AND TRADEMARK OFFICE

# BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte RUSSELL M. MEDFORD and CLARENCE F. BENNETT

Appeal No. 1999-1215 Application No. 08/401,192

ON BRIEF

Before WINTERS, ADAMS, and MILLS, <u>Administrative Patent Judges</u>.

ADAMS, <u>Administrative Patent Judge</u>.

#### **DECISION ON APPEAL**

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 35-43, which are all the claims pending in the application.

Claim 35 is illustrative of the subject matter on appeal and is reproduced below:

35. A linear chimeric oligonucleotide for down-regulating expression of a gene comprising a first region having a sequence which is identical to at least a portion of a sequence of said gene, which gene sequence binds a transcriptional regulatory factor, and a second region specifically hybridizable either with a splicing region of pre-mRNA deriving from the gene or with mRNA deriving from the gene.

The references relied upon by the examiner are:

Blumenfeld et al. (Blumenfeld)

WO 92/19732

Nov. 12, 1992

Inoue et al. (Inoue), "Sequence-dependent hydrolysis of RNA using modified oligonucleotide splints and RNase H," <u>FEBS Letters</u>, Vol. 215, No. 2, pp. 327-330 (1987)

Hélène et al. (Hélène), "Specific regulation of gene expression by antisense, sense and antigene nucleic acids," <u>Biochimica et Biohysica Acta</u>, Vol. 1049, pp. 99-125 (1990)

## GROUND OF REJECTION1

Claims 35-43 are rejected under 35 U.S.C. § 103 as being unpatentable over Hélène in view of Blumenfeld and Inoue.

We reverse.

### **DISCUSSION**

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims, and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer<sup>2</sup> for the examiner's reasoning in support of the rejection. We further reference appellants' Brief<sup>3</sup>, and appellants' Reply Brief<sup>4</sup> for the appellants' arguments in favor of patentability.

THE REJECTION UNDER 35 U.S.C. § 103:

<sup>&</sup>lt;sup>1</sup> Rejections not referred to in Answer are assumed to have been withdrawn. <u>Exparte EMM</u>, 118 USPQ 180, 181 (Bd. Pat. App. & Int. 1958). Accordingly, we note the examiner withdrew the rejection of claims 35-43 under 35 U.S.C. § 112, second paragraph.

<sup>&</sup>lt;sup>2</sup> Paper No. 16, mailed September 21, 1998.

<sup>&</sup>lt;sup>3</sup> Paper No. 15, received July 9, 1998.

<sup>&</sup>lt;sup>4</sup> Paper No. 17, received November 24, 1998.

The initial burden of presenting a <u>prima facie</u> case of obviousness rests on the examiner. <u>In re Oetiker</u>, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

According to the examiner (Answer, page 3), Hélène teach linear oligos for inhibition of gene expression. However, Hélène does not teach oligos containing different regions intended to act through different mechanisms. The examiner notes that Blumenfeld teach (Answer, page 3) "circular oligos comprising two regions, an antisense region targeted to a mRNA molecule and a sense region targeted to a (protein) transcription factor." The examiner argues (Answer, page 3) that Blumenfeld "teach that combining the sense and antisense approaches should produce a synergistic effect in inhibiting gene expression." The examiner relies on Inoue to teach (Answer, page 4) "oligo sequences which are cleaved by RNase H."

While a person of ordinary skill in the art may possess the requisite knowledge and ability to modify the linear oligos of Hélène, the modification is not obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 211 USPQ 1125, 1127 (Fed. Cir. 1984). Here we see no such reason to modify the references as applied. In fact, the Blumenfeld reference, relied upon by the examiner (Answer, page 4) to teach chimeric

oligos, teaches away from using linear oligos. Blumenfeld teach (title) "closed sense and antisense oligonucleotides." Blumenfeld teach (pages 13-14):

Modifications made to the structure of the ends of antisense oligonucleotides can protect them, block the activities of the exonucleases, and increase the stabilization of the oligonucleotides.

The invention described here is based on the novel idea that closed oligonucleotides, without free ends, would thus be ... by definition, resistant to this type of degradation. Closed oligonucleotides, for example, circular oligonucleotides, do not present a substrate which is accessible to 3' or 5' exonucleases, and they are thus stabilized.

Thus, as suggested by appellants (Brief, page 5) "[t]he Blumenfeld authors ... were not motivated to linearize their oligonucleotides notwithstanding that they clearly possessed knowledge of the facts alleged to motivate such a modification. As argued by appellants (Brief, page 6) "[t]hroughout the Blumenfeld reference, its authors describe the advantages of using closed oligonucleotides."

Therefore, we cannot agree with the examiner's contention (Answer, page 6) "that the skilled artisan, being thoroughly familiar with the synthesis and use of linear oligos, would read Blumenfeld et al. and recognize a good idea – using two mechanisms of inhibition at once – which would be equally applicable to standard linear oligos as to closed oligos." Just as one of ordinary skill in this art would recognize in Blumenfeld the advantage of using two mechanisms of inhibition at once, this artisan would also recognize the advantage of using closed oligos instead of linear oligos. We remind the examiner that as stated in Panduit Corporation v. Dennison Manufacturing Co., 774 F.2d 1082, 1093, 227 USPQ 337, 344 (Fed. Cir. 1985) "[t]he well established rule of law is that each prior art reference must be evaluated as an entirety, and that all of the prior art

must be evaluated as a whole." See W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984); In re Kuderna, 426 F.2d 385, 390, 165 USPQ 575, 578-79 (CCPA 1970). Furthermore, "it is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art." In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965); see also In re Mercer, 515 F.2d 1161, 1165-66, 185 USPQ 774, 778 (CCPA 1975).

To establish a <u>prima facie</u> case of obviousness, there must be more than the demonstrated existence of all of the components of the claimed subject matter. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge cannot come from the applicants' disclosure of the invention itself. <u>Diversitech Corp. v. Century Steps, Inc.</u>, 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); <u>In re Geiger</u>, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); <u>Interconnect Planning Corp. v. Feil</u>, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). On the record before us, we find no reasonable suggestion for combining the Blumenfeld teachings of the advantages of using a circular oligo's with two regions with the teaching of Hélène drawn to single region linear oligos.

Inoue's teaching of oligo sequences cleaved by RNase H fails to make up for the deficiencies in the combination of Hélène in view of Blumenfeld.

The initial burden of presenting a <u>prima facie</u> case of obviousness rests on the examiner. <u>In re Oetiker</u>, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On this record, the examiner failed to provide the evidence necessary to support a <u>prima facie</u> case of obviousness.

Accordingly, the rejection of claims 35-43 under 35 U.S.C. § 103 over Hélène in view of Blumenfeld and Inoue is reversed.

## **REVERSED**

| SHERMAN D. WINTERS<br>Administrative Patent Judge | )<br>)<br>)                                  |
|---|--|
| DONALD E. ADAMS<br>Administrative Patent Judge    | )<br>) BOARD OF PATENT<br>)<br>) APPEALS AND |
|   | )<br>) INTERFERENCES                         |
| DEMETRA J. MILLS Administrative Patent Judge      | )<br>)                                       |

Application No. 08/401,192

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